# Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options

# September 21, 2013 Meeting Summary

## Overview

On September 21, 2013, the 21-member Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options convened in Washington, D.C. for their second in-person meeting. The panel includes caregivers, patient-caregiver advocates, clinicians, researchers, organizational providers, and representatives from payers, industry and purchasers.

The panelists met to address 2 of the 4 high-priority research topics that were identified in April during the first advisory panel meeting: Bipolar Disorder and Antipsychotic Use in Adolescents and Young Adults and Ductal Carcinoma in Situ (DCIS). Prior to the meeting, panelists received research reports describing the problem and state of current knowledge for each topic.

The overall goal for the panel's consideration of these two topics was to work with stakeholders to help PCORI identify, refine, and prioritize research evidence gaps. After extensive discussion, panelists used a software tool provided by the RTI-UNC Evidence Based Practice Center to inform their prioritization of specific research questions.

The panel also heard updates from a task force created to follow-up on exploratory work by PCORI on the topic of low back pain. Representatives from the task force updated the panel on their progress and findings.

Later, panelists discussed the overall research portfolio and made suggestions for enhancing its impact and accelerating potentially high-impact research.

# Background

David Hickam, MD, MPH, Program Director for the Clinical Effectiveness Research* Program, began the meeting with an overview of PCORI's topic generation and research prioritization process. In August of 2012, PCORI began collecting research topics from patients and stakeholders via the PCORI website and through workgroups and roundtables. Over 1,300 topics were received, 594 of which were assigned to the Clinical Effectiveness Research Program. These topics were screened, consolidated and evaluated against four criteria:

**1) Patient-centeredness.** Is the proposed research focused on questions and outcomes of specific interest to patients, their caregivers, and clinicians?

**2) Burden.** Is the condition or disease associated with a significant burden in the US population (in terms of prevalence, mortality, morbidity, individual suffering, or loss of productivity)? Alternatively, is it a rare disease with significant clinical impact?

**3) Potential for improving healthcare practice.** What is the likelihood that this research will change clinical practice or clinical decision making?

**4) Timeliness.** Are potential projects associated with this topic likely to be accomplishable within a short time frame (three to five years)?

In April of 2013, the 20 highly rated topics were considered and prioritized by the Assessment of Prevention, Diagnosis, and Treatment Options Advisory Panel. The panel identified four as high priority topics that should be further explored for PCORI research funding program:

- **Bipolar disorder**—Compare the effectiveness of medication regimens for adolescents and young adults with bipolar disorder.
- **Ductal Carcinoma in situ**—Compare the effectiveness of management strategies for ductal carcinoma in situ among women who had this diagnosis made after undergoing screening mammography.
- **Migraine headache**—Compare the effectiveness of treatment strategies for adults with episodic and chronic migraine headaches.
- **Osteoarthritis**—Compare the effectiveness of alternative strategies for stabilizing symptoms in people with osteoarthritis.

On September 21, 2013, the panel convened for a second in person meeting to further discuss the important research gaps for ductal carcinoma in situ and bipolar disorder and prioritize high priority research questions for both topics.

*The Assessment of Prevention, Diagnosis, and Treatment Options Program changed its name to Clinical Effectiveness Research Program in August 2013.

### Topics for Research Prioritization Reviewed at April 19-20, 2013 Meeting

Topic 1: Attention Deficit Hyperactivity Disorder (ADHD)
Topic 2: Bipolar Disorder
Topic 3: Hip fracture
Topic 4: Carotid Artery Disease
Topic 5: Cerebral Adrenoleukodystrophy (ALD)
Topic 6: Coronary Artery Disease
Topic 7: Ductal Carcinoma
Topic 8: Gestational Diabetes
Topic 9: Eczema
Topic 10: Epilepsy
Topic 11: Generalized Anxiety Disorder (GAD)
Topic 12: Hearing loss
Topic 13: Chronic Kidney Disease
Topic 14: Treatments for liver cancer
Topic 15: Macular Degeneration
Topic 16: Melanoma
Topic 17: Migraine headache
Topic 18: Multiple Sclerosis
Topic 19: Obstructive Sleep Apnea
Topic 20: Osteoarthritis

### Highest Priority Research Topics Identified at April 19-20, 2013 Meeting

- Bipolar Disorder and Antipsychotic Use in Adolescents and Young Adults
- Ductal Carcinoma in Situ
- Osteoarthritis
- Migraine headaches

### Research Topics Discussed at September 21, 2013 Meeting

- Bipolar Disorder and Antipsychotic Use in Adolescents and Young Adults
- Ductal Carcinoma in Situ

## Discussion

The discussion of the important research gaps in the topic areas of ductal carcinoma and bipolar disorder and antipsychotic use in adolescents and young adults began with background presentations from Evan R. Myers, MD, MPH, and Matt Crowley, MD, from the Duke Evidence Synthesis Group. Following the presentations, panel members discussed the important research gaps in the two topic areas.

Key discussion points for DCIS included:

**Risk stratification and the natural history of DCIS.** Panelists stressed the importance of new knowledge to support informed decisions around treatment options for patients. The natural history of DCIS is currently unknown; patients face considerable uncertainty about the implications of alternative treatments. The advisory panel agreed that DCIS research should be aimed at improving information with which patients make decisions. They also concluded that a better understanding of the comparative outcomes of aggressive treatment of DCIS versus watchful waiting is needed.

**Communicating risk.** Understanding how communicating risk to patients changes the choice of treatment was identified as another important research topic. Panelists noted that the framing of a diagnosis can affect patient outcomes, and also that the question of how we make decisions in the face of uncertainty is one that can be addressed in a relatively short timeframe, making it a good prospect for PCORI funding.

Key discussion points for Bipolar Disorder in Adolescents and Young Adults included:

**Consideration of Patient-Centered Outcomes.** The panel expressed the need for research to address patient-centered outcomes such as social and academic functioning.

**Diagnostic uncertainty and disparities in diagnosis.** The diagnosis of Bipolar Disorder in adolescents is highly debated and the accuracy of diagnosis is often uncertain. Panelists expressed concern that treatment in the face of diagnostic uncertainty can lead to negative outcomes for the patient. Panelists also acknowledged that patient socio-demographic characteristics and race/ethnicity can lead to disparities in the diagnosis of Bipolar Disorder in adolescents. While panelists identified that reducing this uncertainty was important, they acknowledged that this did not need to be a separate research topic but should be addressed within PCORI-funded research.

**Treatment comparisons.** Panel members discussed the possible benefit of investigating the use of medication in conjunction with other therapies, such as psychotherapy. They articulated the need to understand the relative contributions of psychotherapy and drug treatment, as well as the differences between mono- (single mode) therapies and combination therapies.

**Adherence to medication.** Panelists agreed that improving adherence to medication is a high priority area for research topic, especially in terms of how the choice of medication affects adherence, and how adherence effects outcomes.

Other items discussed at the meeting included:

**Update on the low back pain topic.** PCORI conducted initial exploratory work on the topic of low back pain in spring 2013. A task force carried out follow-up work, and two panelists who served on the task force, Regina Dehen and Harold Sox, shared their findings with the panel. Task force discussions with stakeholders, including several federal agency representatives, helped to clarify the key questions and identify data gaps. The main insights emerged from those discussions were that the progression of back pain from acute to chronic was a critical transition to understand through research and that developing interventions based on those risks of progression was also key.

**Overview of the Assessment of Options portfolio.** Panel members provided input on the PCORI research portfolio in the assessment of prevention, diagnosis, and treatment options. Members mentioned the need for separate inclusion of the pediatric population; the importance of dissemination of information of PCORI-funded research; considering the contribution to advancing methodology in specific research areas when ranking topics, and the importance of learning how to use large data sets.

## Action

Panelists used the RTI International-University of North Carolina at Chapel Hill (RTI-UNC) Evidence Based Practice Center prioritization software to process their priority ratings of research questions, in some cases grouping several related questions together as they “scored” the questions.

The most highly ranked research questions for Ductal Carcinoma in Situ were:

- Combination of the following two questions:
    a. Is it possible to develop and validate risk stratification models based on currently available data on patient characteristics, clinical characteristics, and test results that accurately identify subsets of women with DCIS for whom the balance of benefits and harms is relatively clear for specific intervention strategies, including (a) observation/active surveillance only, (b) local excision only, (c) local excision with radiation therapy, and (d) mastectomy?
    b. Do the comparative safety and effectiveness of management strategies (including observation/active surveillance) for women diagnosed with DCIS differ depending on variations in **clinical, pathologic, and genomic presentations of DCIS** (e.g., grade, topographic nature of tumor, positive margins, pN0(i+) or pN1mic SLN metastases)?

- Combination of the following three questions:
    a. What are the comparative safety and effectiveness of a management strategy involving no immediate treatment (i.e., observation/active surveillance) versus immediate treatment with surgery, radiation, and/or medical therapy? For women who choose observation/active surveillance, what is the optimal frequency and length of observation/active surveillance? Are outcomes different for women who elect observation/active surveillance and subsequently have an invasive cancer detected and treated compared to women who choose immediate treatment for DCIS?
    b. What is the impact of DCIS management strategies on **comorbidities**?
    c. What is the impact of DCIS management strategies on rates of **invasive cancers**?

- Combination of the following two questions:
    a. What is the comparative effectiveness of different approaches to communicating the diagnosis of DCIS to the patient (e.g., 'cancer' vs. 'non-invasive cancer' vs. 'pre-cancer,' likelihood of progression to invasive cancer, time frame/urgency for making management decisions) in terms of (a) choices patients make about which specific

    management strategies (including observation/active surveillance) to use, and when to start them, and (b) outcomes related to these decisions, including patient satisfaction, decisional regret, anxiety, distress/confusion, or other key patient-centered outcomes?
    b. What is the comparative effectiveness of **decision making tools** compared to **usual care** in terms of (a) choices patients make about which specific management strategies (including observation/active surveillance) to use, and when to start them, and (b) outcomes related to these decisions, including patient satisfaction, decisional regret, anxiety, distress/confusion, or other key patient-centered outcomes? What are the optimal format, content, and timing for these decision aids? How consistently are these decision tools used in practice?

The most highly ranked research questions for Bipolar Disorder and Antipsychotic Use in Adolescents and Young Adults were:

- Combination of the following two questions:
    a. What are the comparative effects of antipsychotics on social, academic, and occupational functioning in adolescents/young adults with bipolar disorder?
    b. What are the **key patient-centered and family-centered outcomes** for adolescents/young adults with bipolar disorder and their families, and how are these outcomes affected by different antipsychotic classes/agents?

- Combination of the following three questions:
    a. What are the comparative safety and effectiveness of monotherapy compared to combination therapy with antipsychotic drugs in adolescents/young adults with bipolar disorder?
    b. What are the comparative safety and effectiveness of **'mood stabilizing' medication classes** (e.g., lithium or antiepileptic drugs like lamotrigine or valproic acid) compared with antipsychotic drugs in adolescents/young adults with bipolar disorder?
    c. What are the comparative safety and effectiveness of using **specific antipsychotic classes/agents** (e.g., 1st generation compared with 2nd generation antipsychotics) in adolescents/young adults with bipolar disorder?

- Combination of the following two questions:
    a. How do the comparative safety and effectiveness of antipsychotic treatment in adolescents/young adults with bipolar disorder differ depending on demographic differences such as age group (e.g., under 18 versus 18-25), rural versus urban, race/ethnicity, and sex?
    b. How do the comparative safety and effectiveness of antipsychotic treatment in adolescents/young adults with bipolar disorder differ depending on **socioeconomic**

**factors** such as income, insurance status, access to healthcare and to types of services, and level of caregiver/social support?

## Next Steps

The next Advisory Panel meeting will be held on January 13-14th in Washington, DC. The purpose of this meeting will be to discuss and prioritize research gaps for the migraine headache and osteoarthritis topics as well as prioritize new research topics.